Claims

1. A method for obtaining a natural product from plant material, the method comprising:

(a) contacting plant material with a solvent to provide a first mixture;

(b) separating the plant material from the solvent to provide a first extract;

(c) contacting the first extract with an aqueous base to provide a second mixture;

(d) heating the second mixture in a solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C; effective to distill off water present in the second mixture, thereby providing a third mixture;

(e) separating solids from the third mixture to provide a fourth mixture;

(f) contacting the fourth mixture with a binder, thereby providing a fifth mixture;

(g) concentrating the fifth mixture, or precipitating solids from the fifth mixture, to provide a natural product.

2. The method of claim 1 wherein more than one natural product is obtained.

3. The method of claim 1 wherein at least one of betulin, betulinic acid, and lupeol are obtained.

4. The method of claim 1 wherein the natural product obtained is betulin, in a purity of at least about 95 wt.%.

5. The method of claim 1 wherein the natural product obtained is betulin, and wherein the betulin includes betulinic acid in a weight ratio of at least about 5,000:1, of betulin to betulinic acid.

6. The method of claim 1 wherein the natural product obtained is betulin, and wherein the betulin includes betulinic acid in a weight ratio of at least about 10,000:1, of betulin to betulinic acid.

7. The method of claim 1 wherein the natural product obtained is betulin, and wherein the betulin includes betulinic acid in an amount of up to about 0.02 mol. %.

8. The method of claim 1 wherein the precipitating of the solids from the fourth mixture provides the natural product and a mother liquor.

9. The method of claim 1 wherein the precipitating of the solids from the fourth mixture provides betulin, and a mother liquor that comprises lupeol.

10. The method of claim 1 wherein, in step (e), the solids separated from the third mixture comprise betulinic acid.

11. The method of claim 1 wherein the plant material employed comprises birch bark.

12. The method of claim 1 wherein the plant material employed comprises inner birch bark.

13. The method of claim 1 wherein the plant material employed comprises outer birch bark.

14. The method of claim 1 wherein the plant material employed comprises birch bark pellets.

15. The method of claim 1 wherein the plant material employed comprises at least about 150 kg of birch bark.

16. The method of claim 1 wherein the plant material employed comprises at least about 2,000 kg of birch bark.

17. The method of claim 1 wherein the plant material employed comprises *Betula papyrifera*, *Betula pendula*, or a combination thereof.

18. The method of claim 1 wherein the plant material employed comprises Tanzanian Tree Uapaca nitida Mull-Arg (Euphorbiacea), leaves and/or bark of Bacopa monniera (West Bengal), Dilleniacea (Acrotrema arnothianum Wight), Dillenia andamanica Parkinson, D. aurea Smith, D. bracteata Wight, D. indica Linn, D. pentagina Roxb, D. retusa Thunb, D. scabtalla (D. Don) Roxb, exWall, Tetracera (Houtt. exChrism.& Panz., Merr.), Tetracera akara (Burm.f.) Merr., T. indica (Houtt. exChrism.& Panz., Merr.), T. sarmentosa (L.) Vahl. Subsp. Andamanica (Hoogl.) Hoogl., T. scandens (L.) Merr, or any combination thereof.

19. The method of claim 1 wherein the solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C, in step (d) comprises an optionally substituted aromatic hydrocarbon.

20. The method of claim 1 wherein the solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C, in step (d) comprises at least one of xylene, toluene, and benzene.

21. The method of claim 1 wherein the contacting in step (a) is further accompanied by heating the first mixture.

22. The method of claim 1 wherein the contacting in step (a) is further accompanied by heating the first mixture above about 90°C.

23. The method of claim 1 wherein the contacting in step (a) is further accompanied by heating the first mixture to reflux.

24. The method of claim 1 wherein the contacting in step (a) is further accompanied by heating the first mixture for more than about 30 minutes.

25. The method of claim 1 wherein the separating in step (b) includes filtering the first mixture, decanting the first mixture, or a combination thereof.

26. The method of claim 1 wherein the separating in step (b) comprises filtering the first mixture, decanting the first mixture, or a combination thereof; wherein the temperature of the first mixture is above about 70°C.

27. The method of claim 1 wherein the separating in step (b) comprises filtering the first mixture, decanting the first mixture, or a combination thereof; and washing any solids obtained with a water-immiscible solvent.

28. The method of claim 1 wherein the separating in step (b) comprises filtering the first mixture, decanting the first mixture, or a combination thereof; and washing any solids obtained with a water-immiscible solvent having a temperature of up to about 110°C.

29. The method of claim 1 wherein the separating in step (b) comprises filtering the first mixture, decanting the first mixture, or a combination thereof; and washing any solids obtained with xylenes.

30. The method of claim 1 further comprising, after step (b), concentrating the first extract.

31. The method of claim 1 wherein the aqueous base comprises an alkaline metal or an alkaline earth metal.

32. The method of claim 1 wherein the aqueous base comprises a lithium ion (Li^+), a sodium ion (Na^+), a potassium ion (K^+), a calcium ion (Ca^{2+}), a barium ion (Ba^+), an alkyl ammonium ion ($R^1R^2R^3R^4N^+$), wherein each of R^1-R^4 is independently (C_1-C_{20}) alkyl, optionally substituted with one or more of halo, cyano, nitro, alkoxy, amino, or trihaloalkyl; or any combination thereof.

33. The method of claim 1 wherein the aqueous base comprises at least one sodium hydroxide (NaOH) and potassium hydroxide (KOH).

34. The method of claim 1 wherein, in step (d), the second mixture is heated at a temperature and for a period of time, effective to distill off water present in the second mixture and to hydrolyze natural esters of the natural product.

35. The method of claim 1 wherein, in step (d), the second mixture is heated to reflux.

36. The method of claim 1 wherein, in step (d), the water is distilled off azeotropically with the water-immiscible solvent.

37. The method of claim 1 wherein, in step (d), up to about 100 wt.% of the water is azeotropically distilled off.

38. The method of claim 1 wherein, in step (d), more than about 95 wt.% of the water is azeotropically distilled off.

39. The method of claim 1 wherein, in step (d), the heating is further accompanied by agitating the second mixture.

40. The method of claim 1 wherein, in step (d), the heating is further accompanied by vigorously stirring the second mixture.

41. The method of claim 1 wherein the solvent in step (a) is water-miscible, and the water-miscible solvent is subsequently removed, prior to the heating in step (d).

42. The method of claim 1 wherein the solvent in step (a) is water-immiscible, and the water-immiscible solvent is present during the heating, in step (d).

43. The method in claim 1 wherein the separating comprises filtering, decanting, or a combination thereof.

44. The method in claim 1 wherein, in step (e), the solids that are separated from the third mixture comprise betulinic acid.

45. The method of claim 1 wherein the separating in step (e) includes filtering the third mixture, decanting the third mixture, or a combination thereof.

46. The method of claim 1 wherein the separating in step (e) includes filtering the third mixture, decanting the third mixture, or a combination thereof; wherein the temperature of the third mixture is above about 70°C.

47. The method of claim 1 wherein the separating in step (e) includes filtering the third mixture, decanting the third mixture, or a combination thereof; and washing any solids obtained with a water-immiscible solvent.

48. The method of claim 1 wherein the separating in step (e) includes filtering the third mixture, decanting the third mixture, or a combination thereof; and washing any solids obtained with a water-immiscible solvent having a temperature of up to about 110°C.

49. The method of claim 1 wherein the separating in step (e) includes filtering the third mixture, decanting the third mixture, or a combination thereof; and washing any solids obtained with xylenes.

50. The method of claim 1 wherein the fourth mixture comprises a binder selected from the group of metal hydrides, metal alcoholates, ortho-esters and dialkoxysulfates, and combinations thereof.

51. The method of claim 1 wherein the fourth mixture comprises a binder selected from the group of lithium hydride (LiH), sodium hydride (NaH), potassium hydride (KH), calcium hydride (CaH_2), and lithium aluminum hydride ($LiAlH_4$).

52. The method of claim 1 wherein the fourth mixture comprises a binder selected from the group of sodium methoxide (NaOMe), sodium ethoxide (NaOEt), potassium methoxide (KOMe), potassium ethoxide (KOEt), aluminum *iso*-propoxide [$Al(i\text{-}PrO)_3$], aluminum *tert*-butoxide [$Al(t\text{-}BuO)_3$], aluminum ethoxide ($Al(OEt)_3$), aluminum propoxide ($Al(OPr)_3$, aluminum butoxide ($Al(OBu)_3$), and aluminum methoxide [$Al(OMe)_3$].

53. The method of claim 1 wherein the fourth mixture comprises a binder selected from the group of ethylorthocarbonate, dimethylsulfate, and diethylsulfate.

54. The method of claim 1 wherein, in step (f), the concentrating of the fourth mixture is carried out at a pressure of up to about 1 atm.

55. The method of claim 1 wherein the amount of natural product obtained, based on the amount of the first extract obtained in step (b), is at least about 65 wt.%.

56. The method of claim 1 that provides about 40 wt.% to about 65 wt.% of betulin, based upon the amount of concentrated first extract.

57. The method of claim 1 that provides about 10 wt.% to about 25 wt.% of betulin, based upon the amount of the plant material employed.

58. The method of claim 1 that provides about 2 wt.% to about 5 wt.% of lupeol, based upon the amount of concentrated first extract.

59. The method of claim 1 that provides about 2 wt.% to about 5 wt.% of betulinic acid, based upon the amount of concentrated first extract.

60. A method for obtaining betulin from birch bark, the method comprising:

(a) contacting birch bark with a solvent to provide a first mixture;

(b) separating the birch bark from the solvent to provide a first extract;

(c) contacting the first extract with an aqueous base to provide a second mixture;

(d) heating the second mixture in solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C; effective to distill off water present in the second mixture, thereby providing a third mixture;

(e) separating solids from the third mixture to provide a fourth mixture; and

(f) concentrating the fourth mixture to provide betulin, or precipitating betulin from the fourth mixture.

61. A method for obtaining lupeol from birch bark, the method comprising:

(a) contacting birch bark with a solvent to provide a first mixture;

(b) separating the birch bark from the solvent to provide a first extract;

(c) contacting the first extract with an aqueous base to provide a second mixture;

(d) heating the second mixture in a solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C; effective to distill off water present in the second mixture, thereby providing a third mixture;

(e) separating solids from the third mixture to provide a fourth mixture;

(f) contacting the fourth mixture with a binder to provide a fifth mixture;

(g) concentrating the fifth mixture, or precipitating solids from the fifth mixture;

(h) filtering any solids from the fifth mixture to provide a mother liquor;

(i) concentrating the mother liquor to provide crude lupeol;

(j) washing the crude lupeol with a polar organic solvent;

(k) recrystallizing the crude lupeol from a non-polar organic solvent; and

(l) recrystallizing the crude lupeol from a polar organic solvent.

62. The method of claim 61, wherein the polar organic solvent in (j) comprises acetone, methyl ethyl ketone, ethyl acetate, or any combination thereof.

63. The method of claim 61, wherein the non-polar organic solvent in (k) comprises cyclohexane, hexane, heptane, hexanes, toluene, benzene, p-xylene, m-xylene, o-xylene, trifluoromethylbenzene, or any combination thereof.

64. The method of claim 61, wherein the polar organic solvent in (l) comprises acetone, methyl ethyl ketone (MEK), ethyl acetate, methanol, ethanol, or any combination thereof.

65. A method for obtaining betulinic acid from birch bark, the method comprising:

(a) contacting birch bark with a solvent to provide a first mixture;

(b) separating the birch bark from the solvent to provide a first extract;

(c) contacting the first extract with an aqueous base to provide a second mixture;

(d) heating the second mixture in a solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C; effective to distill off water present in the second mixture, thereby providing a third mixture;

(e) separating solids from the third mixture;

(f) washing the solids with water;

(g) neutralizing or acidifying the solids in an aqueous acid, thereby providing a fourth mixture;

(h) separating betulinic acid from the fourth mixture;

(i) crystallizing the betulinic acid with a polar organic solvent; and

(j) optionally drying the betulinic acid.

66. The method of claim 65, wherein the acid in (g) comprises H_2SO_4, HCl, H_3PO_4, HNO_3, HNO_2, H_3PO_3, CH_3COOH, CF_3COOH, H_3SO_3, or any combination thereof.

67. The method of claim 65, wherein the polar organic solvent in (i) comprises CH_3OH, EtOH, PrOH, i-PrOH, BuOH, t-BuOH, sec-BuOH, $C_5H_{11}OH$, acetone, ethyl acetate, methylethyl ketone (MEK), diethyl ketone, or any combination thereof.

68. A method for purifying an extract of a natural product, the method comprising:

(i) contacting an extract of a natural product with an aqueous base, to provide a first mixture;

(ii) heating the first mixture in a solvent that: (i) is water-immiscible, (ii) is capable of forming an azeotropic mixture with water, or (iii) has a boiling point of at least 100°C; effective to distill off water present in the first mixture, thereby providing a second mixture;

(iii) separating solids from the second mixture, to provide a third mixture; and

(iv) concentrating the third mixture or precipitating solids from the third mixture, to provide a purified natural product.

69. The compound obtained from the method of any one of claims 1-68.

70. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound of claim 69.

71. A cosmetic composition comprising a cosmetically acceptable carrier and the compound of claim 69.